DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 201,341, and 369

[Docket Nos. 98N–0337, 96N–0420, 95N–0259, 90P–0201]

RIN 0910–AA79

Over-The-Counter Human Drugs; Labeling Requirements; Final Rule; Technical Amendment

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; technical amendment.

SUMMARY: The Food and Drug Administration (FDA) is amending the regulation that established a standardized format and standardized content requirements for the labeling of over-the-counter (OTC) drug products, and is amending several related OTC drug product labeling regulations. This amendment corrects and conforms several aspects of the new labeling requirements to other regulatory provisions and eliminates unnecessary text from the new labeling regulation.

DATES: This regulation is effective *[insert date of publication in the* **Federal Register].** Submit written comments by *[insert date 75 days after date of publication in the* **Federal Register].**

ADDRESSES: Submit written comments to the Dockets Management Branch **(HFA–305),** Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Cazemiro R. Martin or Gerald M. Rachanow, Center for Drug Evaluation and Research **(HFD–560),** Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2222.

SUPPLEMENTARY INFORMATION:

I. Background

In **the Federal Register** of March 17, 1999 (64 FR 13254), FDA published a final rule establishing a standardized format and standardized content requirements for the labeling of OTC drug products. The final rule is codified primarily in § 201.66 (21 CFR 201.66). The rule was effective on May 16, 1999 (64 FR 18571, April 15, 1999), but is subject to a detailed implementation plan outlined in the final rule (64 FR 13254 at 13273 to 13274).

II. Technical Amendments

1. Section 201.66(c) states that the information in paragraphs (c)(1) through (c)(8) must appear in the order listed. Section 201.66(c)(5)(ii)(A) contains the "Allergy alert" warning, followed by § 201.66(c)(5)(ii)(B), which contains the ' 'Reye's syndrome" warning required under § 201.314(h)(l) (21 CFR 201.314(h)(l)). The order in § 201.66(c)(5)(ii) is not consistent with another FDA labeling provision.

Under § 201.314(h)(2), the Reye's syndrome warning must be the first warning listed under the "Warnings" heading. To conform § 201.66(c)(5)(ii) to § 201.314(h)(2), the agency is redesignating paragraph (c)(5)(ii)(A) as paragraph (c)(5)(ii)(B) and paragraph (c)(5)(ii)(B) as paragraph (c)(5)(ii)(A). In addition, the agency is correcting the word "Reye" to read "Reye's" in § 201.314(h)(1).

2. Section 201.66(c)(5)(iii) requires the use of the subheading "Do not use." Section 330.1(i)(38) (21 CFR 330.1(i)(38)) allows the phrases "give to" and "use in" to be used interchangeably. However, § 201.66(f) does not allow the use of interchangeable terms in subheadings. This limitation on the use of interchangeable terms may cause some confusion when applied to certain monoamine oxidase inhibitor warnings.

Specifically, the monoamine oxidase inhibitor (MAOI) warning in §§ 341.74(c)(4)(vi) (21 CFR 341.74(c)(4)(vi)) and 341.80(c)(1)(ii)(D) (21 CFR 341.80(c)(1)(ii)(D)) provides slightly different

language for products labeled only for children under 12 years of age. The warning states: "Do not give to a child who * * *''. Similarly, the warning under the entry "SODIUM GENTISATE" in § 369.21 (21 CFR 369.21) contains a warning that states "Do not give to children * * *''. To allow these warnings to conform to the required subheadings in the new labeling format, the agency is revising these warnings to replace the words "give to" with the words "use in."

3. Section 201.66(d)(3) of the final rule provides, in relevant part, that the title, headings, subheadings, and information in paragraphs (c)(1) through (c)(9) must not appear in reverse type, and that the required labeling must be all black or one dark color, printed on a white or other light; neutral color, contrasting background. Section 201.66(d)(3) also provides for the use of a single, alternative, contrasting dark color to highlight the Drug Facts title and headings.

Section 201.66(d)(3) is based on the finding that color contrast between text and background is a significant factor affecting the legibility of OTC drug product labeling. Generally, high contrast between the color of the text and the color of the background can significantly improve legibility. If, however, the text blends into the background, consumers may have difficulty focusing on and reading the information.

The final rule recognizes that black text on a white background is the most common way to achieve high contrast. However, to emphasize the importance of contrast and to provide more options than black on white labeling, the agency included the terms "dark" text and "light" background in § 201.66(d)(3). After receiving several inquiries from manufacturers about the meaning of these terms, the agency has decided that the rule would be less confusing if the terms ''dark,'' ''light," and "reverse type" (i.e., "light" type on a "dark" background) were deleted.

Section 201.66(d)(3) is intended to ensure adequate contrast between text and background. The terms "dark' ' and "light" may have added an unnecessary element of complexity to the rule. Aside from the difficulty in assigning a fixed meaning to these terms, the agency acknowledges that there may be combinations of light text on a dark background that, assuming high contrast, would be consistent with achieving readable OTC drug product labeling. (See, e.g.,

Ref. 2 at 62 FR 9024 at 9049 (February 27, 1997), noting that in OTC drug labeling white text on a brown background may provide good, readable contrast.)

To eliminate possible confusion, while keeping the emphasis in the final rule on achieving high contrast, the agency is removing the words "dark" and "light" and the phrase "shall not appear in reverse type" from § 201.66(d)(3). Thus, the amended version of the rule requires black on white text or, any other combination of a single color of text on a contrasting background. Generally, the agency expects the color contrast used in the Drug Facts labeling to be at least as high as that used in a product's principal display panel or other promotional labeling.

These amendments institute minor changes and corrections to the rule and may provide greater flexibility in the implementation of the new OTC drug labeling requirements. Also, with respect to the third technical amendment, the agency notes that only few comments submitted during the rulemaking process addressed the issue of color contrast. Of these, most supported the need for using good contrast but did not take a substantive position on whether to require only dark on light labeling. As discussed above, the agency is retaining the contrast requirement. Therefore, the agency believes this amendment does not present a significant or controversial issue that warrants further opportunity for notice and comment rulemaking.

For these reasons, the agency finds for good cause that notice and comment procedures are unnecessary in this instance and that these changes may go into effect immediately (5 U.S.C. 553(b) and (d) and 21 CFR 10.40(c) and (e)). However, in accordance with 21 CFR 10.40(e)(1), the agency will accept comments on these amendments to determine whether they should be modified or revoked.

III. The Paperwork Reduction Act of 1995

FDA analyzed all relevant information collections associated with this rule in the original final rule document (64 FR 13254 at 13274 to 13276). These amendments do not impose any new requirements and, therefore, do not require any further analysis and are not subject to review by the Office of Management and Budget.

IV. Analysis of Impacts

FDA provided a detailed analysis of impacts in the original final rule document (64 FR 13254 at 13276 through 13285). This technical amendment provides several clarifications and allows additional flexibility in the labeling requirements. Thus, no further analysis of impacts is necessary.

V. Environmental Impact

The agency has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither-an environmental assessment nor an environmental impact statement is required.

List of Subjects

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 341

Labeling, Over-the-counter drugs.

21 CFR Part 369

Labeling, Medical devices, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 201,341, and 369 are amended as follows:

PART 201—LABELING

1. The authority citation for 2 1 CFR part 201 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 358, 360, 360b, 360gg-360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264.

2. Section 201.66 is amended by redesignating paragraphs (c)(5)(ii)(A) and (c)(5)(ii)(B) as paragraphs (c)(5)(ii)(B) and (c)(5)(ii)(A), respectively, and revising paragraph (d)(3) to read as follows:

§ 201.66 Format and content requirements for over-the-counter (OTC) drug product labeling.

* * * * *

(d) * * *

(3) The title, heading, subheadings, and information in paragraphs (c)(l) through (c)(9) of this section shall be legible and clearly presented, shall have at least 0.5-point leading (i.e., space between two lines of text), and shall not have letters that touch. The type style for the title, headings, subheadings, and all other required information described in paragraphs (c)(2) through (c)(9) of this section shall be any single, clear, easy-to-read type style, with no more than 39 characters per inch. The title and headings shall be in bold italic, and the subheadings shall be in bold type, except that the word "(continued)" in the title "Drug Facts (continued)" shall be regular type. The type shall be all black or one color printed on a white or other contrasting background, except that the title and the headings may be presented in a single, alternative, contrasting color unless otherwise provided in an approved drug application, OTC drug monograph (e.g., current requirements for bold print in §§ 341.76 and 341.80 of this chapter), or other OTC drug regulation (e.g., the requirement for a box and red letters in § 201.308(c)(1)).

* * * * *

3. Section 201.314 is amended by revising paragraph (h)(l) to read as follows:

5201.314 Labeling of drug preparations containing salicylates.

* * * * *

(h)(l) The labeling of orally or rectally administered over-the-counter aspirin and aspirin-containing drug products subject to this paragraph is required to prominently bear a warning. The

warning shall be as follows: "Children and teenagers should not use this medicine for chicken pox or flu symptoms before a doctor is consulted about Reye's syndrome, a rare but serious illness reported to be associated with aspirin."

* * * * *

PART 341—COLD, COUGH, ALLERGY, BRONCHODILATOR, AND ANTIASTHMATIC DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

4. The authority citation for 21 CFR part 341 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360,371.

5. Section 341.74 is amended by revising paragraph (c)(4)(vi) to read as follows:

§ 341.74 Labeling of antitussive drug products.

* * * * *

(c) * * *

(4) * * *

(vi) *For products containing dextromethorphan or dextromethorphan hydrobromide as identified in $341.14(a)(3) and (a)(4) when labeled only for children under 12 years of age. Drug interaction precaution.* "Do not use in a child who is taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your child's prescription drug contains an MAOI, ask a doctor or pharmacist before giving this product."

* * * * *

6. Section 341.80 is amended by revising paragraph (c)(1)(ii)(D) to read as follows:

§ 341.80 Labeling of nasal decongestant drug products.

* * * * *

(c) * * *

(1) * * *

(ii) * * *

(D) *Drug interaction precaution.* "Do not use in a child who is taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your child's prescription drug contains an MAOI, ask a doctor or pharmacist before giving this product."

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PART 369—INTERPRETATIVE STATEMENTS RE WARNINGS ON DRUGS AND DEVICES FOR OVER-THE-COUNTER SALE

7. The authority citation for 21 CFR part 369 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 371.

8. Section 369.21 is amended by revising the entry for "SODIUM GENTISATE." to read as follows:

§ 369.21 Drugs; warning and caution statements required by regulations.

* * * * *

SODIUM GENTISATE. (See §§ 201.314 and 310.301(a)(2) of this chapter.)

Warning-Do not use in children under 6 years of age or use for prolonged period unless directed by physician.

"Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away,"

If offered for use in arthritis or rheumatism, in juxtaposition therewith, the statement:

Caution-If pain persists for more than 10 days, or redness is present, or in conditions affecting children under 12 years of age, consult a physician immediately.

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Dated: 12/22/99
December 22, 1999

Margaret M. Dotzel
Acting Associate Commissioner for Policy

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